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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/535,763

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Stefan Werner

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ALSTON & BIRD LLP

BANK OF AMERICA PLAZA

101 SOUTH TRYON STREET, SUITE 4000

CHARLOTTE, NC 28280-4000

EXAMINER

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/535,763	Applicant(s) WERNER ET AL.	
	Examiner BRENT PAGE	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 October 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5, 11-14, 17, 18, 23, 25-27 and 29-31 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5, 11-14, 17, 18, 23, 25-27 and 29-31 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>9/2008</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The Reply filed by Applicants on 10/14/2008 is hereby acknowledged. The cancellation of claims 7-8, 15-16, 20-22, 24 and 32-34 without prejudice is hereby acknowledged. Claims 1-5, 11-14, 17, 18, 23, 25-27 and 29-31 are pending and examined upon the merits herein.

Any claim objections or rejections not specifically addressed below are considered hereby withdrawn in response to Applicants arguments when taken together with the claim amendments.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. There remains an embedded hyperlink in paragraph 89. Deleting the "http://" is not sufficient to remove the embedded hyperlink. The occurrence of "www" must also be deleted. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

The Examiner apologizes for misstating the occurrences of the embedded hyperlinks and acknowledges that the single occurrence is in paragraph 89 of the specification.

Claim Rejections - 35 USC § 101

Applicant's arguments, see page 11 or response, filed 10/14/2008, with respect to the claim amendments have been fully considered and are persuasive. The rejection

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of claims 1-5, 11-14, 17-18, 23, 25, 27 and 29-31 under 35 USC 101 as being directed to nonstatutory subject matter has been withdrawn.

Claim Rejections - 35 USC § 112-enablement

Claims 1-5, 11-14, 17-18, 23, 25-27 and 29-31 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the transformation of Nicotiana plants with provectors comprising the NPT II gene, the 5' end of TMV, a movement protein and a viral coat protein, and the introduction of a recombinase using the VirE2 protein system for translocation of the polypeptide into the cell, does not reasonably provide enablement for the transformation of any plant with any intercellular messenger from any plant or animal or any DNA or RNA modifying enzyme as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The claims remain rejected for the reasons of record in the office action mailed out on 04/15/2008 as well as the reasons set forth below.

Applicant's arguments filed 10/14/2008 have been fully considered but they are not persuasive.

Applicant's urge primarily that the claim amendments obviate the rejection on the grounds that the claims have been narrowed involving plants and two protein portions one of which is a site-specific recombinase, a flippase, a resolvase, an integrase, a polymerase, a transposase and a transcription factor and the other of which is a domain

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of a viral movement protein, a domain of a viral coat protein, a domain of a plant or an animal peptide intercellular messenger, or an artificial peptide capable of enabling cell to cell movement (See pages 12-13 of response).

This is not persuasive because the cited art evidences unpredictability in plant protein targeting even with known in vitro translation systems with known targeting and movement signals were used. Additionally, the claims encompass thousands of enzymes and protein domains from literally millions of organism sources, wherein any "intercellular messenger" or artificial peptide "capable" of enabling cell to cell movement is used. The sheer multitude of possible combinations are further rendered unpredictable when animal intercellular messengers are claimed for the introduction of the protein into a plant.

Applicants urge that the specification enables more than just reporter or selection agents as proteins of interest and that the specification demonstrates systems other than the VirE2 system for translocation (see pages 13-14 of response).

This is not persuasive because the examples and guidance of the specification does not extend to any "intercellular messenger" as broadly claimed, nor does the specification provide guidance for the use of any polymerases or transcription factors as broadly claimed. Specific polypeptides were used in the specification with specific movement polypeptides with no guidance as to which polypeptides are likely to function in plants and which would not apply to plant transformation.

Applicants urge that Mackenzie relates to organelle targeting which is not required in the instant claims (see page 14 of response).

This is not persuasive because the general level of unpredictability is established to demonstrate that when sequences from one environment are introduced into a new environment they do not automatically retain their previous function. This is particularly applicable relating to animal “intercellular messenger”s, but applies to the breadth of the claims generally, as well. Particularly where cell to cell movement is required, and membrane translocation is required, then the signals of organelle signaling would be analogous to other membrane translocation signals.

Applicants urge that the cellular process of interest can be triggered because of the amplification effect achieved by the function of part (i) of claim 1 (page 14 of response).

This is not persuasive because the specification does not provide guidance as to how animal and plant peptide “intercellular messenger”s are capable of cell to cell movement and how they would confer, said movement upon the protein. No sequences are claimed and no sequence consensus is discussed or given in the guidance of the specification as to what confers the ability of a peptide to move from cell to cell.

Claim Rejections - 35 USC § 112-written description

Claims 1-5, 11-14, 17-18, 23, 25-27 and 29-31 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the

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time the application was filed, had possession of the claimed invention. The claims remain rejected for the reasons of record in the office action mailed out on 04/15/2008 as well as the reasons set forth below.

Applicant's arguments filed 10/14/2008 have been fully considered but they are not persuasive.

Applicants urge primarily that the claim amendments obviate the rejection of record and that the claims are not drawn to fragments (pages 15-16 of response).

This is not persuasive with regard to fragments as the claims read on "protein portion" wherein fragments of proteins are analogous and descriptive of the claimed embodiments. This is also not persuasive with regard to the claim amendments in that literally millions if not billions of embodiments encompassing any transcription factor or any polymerase have not been described for causing transcription of heterologous nucleic acid in a plant. Furthermore, the sequences required or the classes required for such transcription have not been described, and thus the full scope of the claims are not full described. The specification also does not describe all plant and animal transcription factors or intercellular messengers that would be capable of cell to cell movement in a plant, or what structural requirements of such factors or messengers are responsible for this function.

Claim Rejections - 35 USC § 102

Claims 1-3, 5, 11-14, 17-18, 23, 25-27, and 29-31 remain rejected under 35 U.S.C. 102(b) as being anticipated by Hookyas et al (WO0189283). The claims remain

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rejected for the reasons of record in the office action mailed out on 04/15/2008 as well as the reasons set forth below.

Applicant's arguments filed 10/14/2008 have been fully considered but they are not persuasive.

Applicants urge that the office action has not clearly stated why Hooykaas et al anticipates the claims and that Hooykaas does not disclose a method of expressing a protein that is capable of leaving a cell, and that the protein expressed is not capable of causing expression of said protein.

This is not persuasive because Hooykaas et al describes a method of controlling a cellular process by providing a plant cell with a fusion protein in which the polypeptide is CRE, an art recognized recombinase and a protein portion using the VirE2 system that is capable of translocating proteins across membranes and thus, cell to cell movement, wherein the recombinase induces transcription of NPTII, the gene of interest which is a heterologous gene. It is noted that a plant or "part thereof" is encompassed by the claims, wherein a part may be a single cell or a tissue of said plant.

Claim Rejections - 35 USC § 103

Claims 1-5, 11-14, 17-18, 23, 25-27 and 29-31 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Klimyuk et al (WO 02/088369) in view of Hooykaas et al (WO 01/89283) and further, in view of Xu et al (WO 00/71701). The claims remain rejected for the reasons of record in the office action mailed out on 04/15/2008 as well as the reasons set forth below.

Applicant's arguments filed 10/14/2008 have been fully considered but they are not persuasive.

Applicants urge primarily that Klimyuk does not teach a protein that is capable of both leaving a cell and entering others and causing expression of said protein in cells containing said heterologous nucleic acid (pages 17-19 of response).

This is not persuasive because Klimyuk et al teach both parts of the protein wherein the viral movement protein and CRE are expressed and CRE is capable of causing the expression of heterologous DNA. The claims do not limit the protein to one that causes its own expression.

Applicants urge that Hooykaas does not teach a protein with both features (i) and (ii) of the claims (pages 19-20 of response).

This is not persuasive because Hooykaas specifically teaches a fusion protein wherein one part is a movement protein and the other part is a recombinase. Hooykaas does not merely teach the introduction of Cre into a cell, but rather a fusion proteins of VirD or VirE with CRE in which both cell to cell movement and recombinase activity are maintained and expressed.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

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Additionally, Applicants urge that Klimyuk does not have the enzymatic activity of a transcription factor (See page 19 of response).

This is not persuasive because the claims are not limited to transcription factors or transcription factor activity. Recombinase activity is also encompassed in the claims.

Applicants urge that Xu et al is essentially unrelated to the invention and does not teach an enzyme having the features of item (ii) (page 20 of response).

This is not persuasive because as discussed above, Applicants may not argue the references individually, but as a whole. This is further not persuasive because intein-based splicing uses fusion proteins where movement proteins are fused with integrase, two features specifically named in the claim limitations.

No claims are free of the prior art.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

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the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BRENT PAGE whose telephone number is (571)272-5914. The examiner can normally be reached on Monday-Friday 8-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on (571)-272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Brent T Page

/Russell Kallis/

Primary Examiner, Art Unit 1638

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